(FILE 'HOME' ENTERED AT 17:42:37 ON 07 MAR 2001)

FILE 'MEDLINE, CANCERLIT, CAPLUS, BIOTECHDS' ENTERED AT 17:43:15 ON 07 MAR 2001

L1 3880 S HEMATOPOIETIC AND GENE THERAPY
L2 12426 S ADENOSINE DEAMINASE
L3 243 S L2 AND L1
L4 ANSWER 48 OF 159 BIOTECHDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1995-08973 BIOTECHDS
TI Post-natal and in utero fetal ***hematopoietic*** stem cell transplantation methods;
adenosine - ***deaminase*** gene expression using a retro virus vector, for application in severe combined immunodeficiency, aplastic anemia, leukemia and hemoglobinopathy therapy
AU Harrison M R; Rice H E
PA Univ.California
PI WO 9512317 11 May 1995
AI WO 1994-US11557 12 Oct 1994
PRAI US 1993-147528 5 Nov 1993
DT Patent
LA English
OS WPI: 1995-193797 [25]
AB The following are claimed: (1) a method for transplanting fetal ***hematopoietic*** stem cells (HSC) into a patient; (2) a method for the ex vivo expansion of fetal HSC; (3) a method for transducing ex vivo expanding fetal HSC with a packaged retro virus; (4) an artificial capillary system (ACS) composed of an ACS cartridge, culture medium containing at least 1 ***hematopoietic*** growth factor, and fetal liver HSC (the culture medium and fetal liver HSC are contained within the cartridge); and (5) a product composed of expanded fetal liver HSC which is separated from other fetal liver cells. The retro virus vector contains a heterologous gene encoding a product; the heterologous gene preferably encodes ***adenosine*** - ***deaminase*** (EC-3.5.4.4). The method further involves transplanting an effective amount of the transduced fetal HSC to a patient suffering from severe combined immunodeficiency. The patient is a fetus and transplantation occurs in utero, or the patient has been born and transplantation occurs

L4 ANSWER 34 OF 159 CAPLUS COPYRIGHT 2001 ACS
AN 1997:644941 CAPLUS
DN 127:314561
TI Long-term in vivo expression of the MFG-ADA retroviral vector in rhesus monkeys transplanted with transduced bone marrow cells
AU Kaptein, Leonie C. M.; Van Beusechem, Victor W.; Riviere, Isabelle; Mulligan, Richard C.; Valerio, Dinko
CS Section Gene Therapy, Department of Molecular Cell Biology, University of Leiden, Leiden, Neth.
SO Hum. Gene Ther. (1997), 8(13), 1605-1610
CODEN: HGTHE3; ISSN: 1043-0342
PB Liebert
DT Journal
LA English
AB We have tested the recombinant human ***adenosine*** ***deaminase*** (hADA) retroviral vector MFG-ADA for its efficacy in transducing hemopoietic stem cells of nonhuman primates and its expression level in the ***hematopoietic*** system. The percentage of provirus-pos.

granulocytes 1 yr after transplantation of bone marrow transduced with MFG-ADA was 0.1%, which was equiv. to previously obtained results with the hADA virus-producing cell line POC-1. However, in MFG-ADA monkeys, significantly more peripheral blood mononuclear cells carried the hADA gene (1% vs. 0.1%). Human ADA expression levels in peripheral blood mononuclear cells were not different between POC-1 and MFG-ADA monkeys using samples with equal nos. of provirus copies per cell. In contrast, in total red blood cell lysates of MFG-ADA monkeys, the hADA expression was higher (.apprx.10-fold) and could be detected longer (20 wk and up to more than 1 yr after bone marrow transplantation in 2 monkeys) than in POC-1 monkeys that were only pos. for up to 12 wk at the most. At 3 yr after bone marrow transplantation, the MFG-ADA provirus could still be detected in 0.1% of bone marrow cells and peripheral blood cells and in 1% of cultured T cells. These results show that MFG-ADA virus can give rise to long-term in vivo expression of hADA in the primate ***hematopoietic*** system. However, transduction efficiencies remain low.

L4 ANSWER 17 OF 159 MEDLINE DUPLICATE 5
AN 1999219789 MEDLINE
DN 99219789
TI ***Gene*** ***therapy*** for severe combined immunodeficiency caused by ***adenosine*** ***deaminase*** deficiency: improved retroviral vectors for clinical trials.
AU Onodera M; Nelson D M; Sakiyama Y; Candotti F; Blaese R M
CS Department of Pediatrics, Hokkaido University School of Medicine, Sapporo, Japan.. mk98d116@md.tsukuba.ac.jp
SO ACTA HAEMATOLOGICA, (1999) 101 (2) 89-96. Ref: 30
Journal code: 0S8. ISSN: 0001-5792.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals; Cancer Journals
EM 199907
EW 19990705
AB Severe combined immunodeficiency (SCID) caused by ***adenosine*** ***deaminase*** deficiency (ADA-) is the first genetic disorder to be treated with ***gene*** ***therapy*** . Since 1990 when the first trial started for 2 patients with ADA- SCID, five clinical trials enrolling 11 patients have been conducted with different clinical approaches and the results obtained from these trials have recently been reported. According to these reports, T cell-directed gene transfer was useful in the treatment of ADA- SCID whereas the retroviral-mediated gene transfer to ***hematopoietic*** stem cells was insufficient for achievement of clinical benefits. This chapter reviews several crucial problems inherent in the current retroviral technology based on the clinical data observed in these pioneering ADA ***gene*** ***therapy*** trials and presents our new retroviral vector system for the next stem cell ***gene*** ***therapy*** .

L4 ANSWER 7 OF 159 MEDLINE DUPLICATE 2
AN 2000236266 MEDLINE
DN 20236266

TI ***Gene*** ***therapy*** for ***adenosine*** ***deaminase*** deficiency.
AU Parkman R; Weinberg K; Crooks G; Nolta J; Kapoor N; Kohn D
CS Division of Research Immunology/Bone Marrow Transplantation, Childrens Hospital Los Angeles, California, USA.. rparkman@chla.usc.edu
NC MO1 RR-43 (NCRR)
DK53041 (NIDDK)
AI40581 (NIAID)
+
SO ANNUAL REVIEW OF MEDICINE, (2000) 51 33-47. Ref: 51
Journal code: 6DR. ISSN: 0066-4219.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200007
EW 20000704
AB The clinical ***gene*** ***therapy*** trials for ***adenosine*** ***deaminase*** (ADA) deficiency have defined both the potential benefits and the present limitations of ***gene*** ***therapy*** with ***hematopoietic*** stem cells (HSC). Current clinical results indicate that (a) both umbilical cord blood and neonatal bone marrow HSC can be transduced with murine retroviral-based vectors, (b) the transduced HSC can engraft in nonmyeloablated patients, (c) the frequency of HSC transduction/engraftment is low (1/10,000), (d) an in vivo selective advantage can exist for transduced T lymphoid progeny, and (e) the transduced ADA gene is not expressed in nondividing T lymphocytes. Improving the clinical results of ***gene*** ***therapy*** for ADA deficiency and other genetic diseases involving HSC will require (a) developing new vectors that express the transduced gene in nondividing cells and (b) increasing the frequency of stable HSC transduction.

L4 ANSWER 6 OF 159 CAPLUS COPYRIGHT 2001 ACS
AN 2000:176430 CAPLUS
DN 132:189222
TI ***Adenosine*** ***deaminase*** deficiency as the first target disorder in ***gene*** ***therapy***
AU Onodera, Masafumi; Sakiyama, Yukio
CS Department of Immunology, Institutes of Basic Medical Sciences, University of Tsukuba, CREST (JST), Tsukuba, Japan
SO Expert Opin. Invest. Drugs (2000), 9(3), 543-549
CODEN: EOIDER; ISSN: 1354-3784
PB Ashley Publications
DT Journal; General Review
LA English
AB A review with 40 refs. In the past decade, the advent of ***gene*** ***therapy*** has been acclaimed as a revolutionary medical intervention, embraced with great enthusiasm. However, recent disappointing results of the considerable clin. trials have also clearly demonstrated that such an initial expectation was an overestimation of ***gene*** ***therapy*** . There are only a few successful cases despite the 3000 patients who have been treated with various forms of ***gene*** ***therapy*** . ***Gene*** ***therapy*** for

severe combined immunodeficiency (SCID) caused by ***adenosine*** ***deaminase*** (ADA) deficiency is one of the few such cases where results have been promising. In particular, peripheral T-lymphocytes-directed ***gene*** ***therapy*** provides further immunol. improvements for patients with ADA-SCID receiving the PEG-ADA treatment whereas ***gene*** ***therapy*** targeting ***hematopoietic*** stem cell has so far proved insufficient for clin. benefits. This report will review crucial problems elucidated in the past five clin. trials for ADA-SCID and gives an outline of the next generation of stem cell ***gene*** ***therapy*** in Japan.

RE.CNT 41

RE

(1) Blaese, R; Science 1995, V270, P475 CAPLUS
(2) Bordignon, C; Science 1995, V270, P470 CAPLUS
(6) Daddona, P; Clin Exp Immunol 1984, V259, P12101 CAPLUS
(7) Daddona, P; J Clin Invest 1983, V72, P483 CAPLUS
(8) Dunbar, C; Blood 1995, V85, P3048 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

LL4 ANSWER 1 OF 159 MEDLINE DUPLICATE 1

AN 2000256141 MEDLINE

DN 20256141

TI ***Gene*** ***therapy*** . The best of times, the worst of times [comment].

CM Comment on: Science 2000 Apr 28;288(5466):669-72

AU Anderson W F

CS Norris Cancer Center, Room 6316, University of Southern California, Keck School of Medicine, 1441 Eastlake Avenue, Los Angeles, CA 90033, USA.. sdiaz@genome2.hsc.usc.edu

SO SCIENCE, (2000 Apr 28) 288 (5466) 627-9.
Journal code: UJ7. ISSN: 0036-8075.

CY United States

DT Commentary
Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals; Cancer Journals

EM 200007

EW 20000701

L4 ANSWER 6 OF 159 CAPLUS COPYRIGHT 2001 ACS
AN 2000:176430 CAPLUS
DN 132:189222
TI ***Adenosine*** ***deaminase*** deficiency as the first target disorder in ***gene*** ***therapy***
AU Onodera, Masafumi; Sakiyama, Yukio
CS Department of Immunology, Institutes of Basic Medical Sciences, University of Tsukuba, CREST (JST), Tsukuba, Japan
SO Expert Opin. Invest. Drugs (2000), 9(3), 543-549
CODEN: EOIDER; ISSN: 1354-3784
PB Ashley Publications
DT Journal; General Review
LA English
AB A review with 40 refs. In the past decade, the advent of ***gene*** ***therapy*** has been acclaimed as a revolutionary medical intervention, embraced with great enthusiasm. However, recent disappointing results of the considerable clin. trials have also clearly demonstrated that such an initial expectation was an overestimation of ***gene*** ***therapy*** . There are only a few successful cases despite the 3000 patients who have been treated with various forms of ***gene*** ***therapy*** . ***Gene*** ***therapy*** for severe combined immunodeficiency (SCID) caused by ***adenosine*** ***deaminase*** (ADA) deficiency is one of the few such cases where results have been promising. In particular, peripheral T-lymphocytes-directed ***gene*** ***therapy*** provides further immunol. improvements for patients with ADA-SCID receiving the PEG-ADA treatment whereas ***gene*** ***therapy*** targeting ***hematopoietic*** stem cell has so far proved insufficient for clin. benefits. This report will review crucial problems elucidated in the past five clin. trials for ADA-SCID and gives an outline of the next generation of stem cell ***gene*** ***therapy*** in Japan.
RE.CNT 41
RE
(1) Blaese, R; Science 1995, V270, P475 CAPLUS
(2) Bordignon, C; Science 1995, V270, P470 CAPLUS
(6) Daddona, P; Clin Exp Immunol 1984, V259, P12101 CAPLUS
(7) Daddona, P; J Clin Invest 1983, V72, P483 CAPLUS
(8) Dunbar, C; Blood 1995, V85, P3048 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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USPT	adenosine deaminase	1442	L6
USPT	hematopoietic stem	1363	L5
USPT,JPAB,EPAB,DWPI	l3 with l1	26	L4
USPT,JPAB,EPAB,DWPI	retrovir$	14207	L3
USPT,JPAB,EPAB,DWPI	heparin	18136	L2
USPT,JPAB,EPAB,DWPI	fibronectin	5231	L1

L4: Entry 2 of 26 File: USPT May 9, 2000

US-PAT-NO: 6060317
DOCUMENT-IDENTIFIER: US 6060317 A

TITLE: Method of transducing mammalian cells, and products related thereto

DATE-ISSUED: May 9, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Malech; Harry L.	Bethesda	MD	N/A	N/A

US-CL-CURRENT: 435/456; 435/304.1, 435/320.1, 435/325, 530/350

CLAIMS:

That which is claimed is:
1. A method of transducing cells comprising:
providing a flexible closed culture container having cells therein; and
contacting said cells with a viral-vector in the presence of a multi-functional chemical moiety, wherein said multifunctional chemical moiety comprises a cell-surface binding domain linked to a virus binding domain, said linkage provided by the surface of the flexible closed culture container.
2. The method of claim 1, wherein said cell-surface binding domain is selected from the group consisting of a cell-surface binding fragment of fibronectin, collagen, vitronectin, thrombospondin, and laminin.
3. The method of claim 2, wherein said cell-surface binding fragment of fibronectin is selected from the group consisting of CBD and CS-1.
4. The method of claim 1, wherein said virus binding domain is selected from the group consisting of a virus binding fragment of fibronectin, virus receptors, and antibodies to env gene products.
5. The method of claim 4, wherein said virus binding fragment of fibronectin is heparin binding domain (III.sub.12-14).
6. The method of claim 1, wherein said viral-vector is selected from the group consisting of herpes simplex virus, adenovirus, adeno-associated virus, lentivirus, and retrovirus vectors.
7. The method of claim 6, wherein said viral-vector is packaged as a pseudotype virus.
8. The method of claim 6, wherein said viral-vector is a retrovirus vector.
9. The method of claim 8, wherein said retrovirus vector is MFGS.
10. The method of claim 1, wherein said cells are hematopoietic cells.
11. The method of claim 10, wherein said hematopoietic cells are CD34+ stem cells.

12. The method of claim 1, wherein said cells are lymphocytes, dendritic cells, or monocytes.
13. The method of claim 1, wherein said contacting occurs in the presence of a polycation.
14. The method of claim 13, wherein said polycation is protamine.
15. The method of claim 1, wherein said contacting occurs in the absence of serum and animal proteins.
16. A container system for transducing cells, comprising a inflexible closed culture container and a multi-functional chemical moiety therein, wherein said multi-functional chemical moiety comprises a cell-surface binding domain linked to a virus binding domain, said linkage provided by the surface of said flexible closed culture container.
17. The system of claim 16, wherein said cell-surface binding domain is selected from the group consisting of a cell-surface binding fragment of fibronectin, collagen, vitronectin, thrombospondin, and laminin.

collagen, vitronectin, thrombospondin, and laminin.
18. The system of claim 17, wherein said cell-surface binding fragment of fibronectin is selected from the group consisting of CBD and CS-1.
19. The system of claim 16, wherein said virus binding domain is selected from the group consisting of a virus binding fragment of fibronectin, virus receptors, and antibodies to env gene products.
20. The system of claim 19, wherein said virus binding fragment of fibronectin is heparin binding domain (III.sub.12-4).

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L4: Entry 4 of 26 File: USPT Apr 18, 2000

US-PAT-NO: 6051427
DOCUMENT-IDENTIFIER: US 6051427 A
TITLE: Method for production of high titer virus and high efficiency retroviral mediated transduction of mammalian cells
DATE-ISSUED: April 18, 2000

US-CL-CURRENT: 435/369; 435/320.1

APPL-NO: 8/ 517488
DATE FILED: August 21, 1995

PARENT-CASE:
CROSS-REFERENCE TO RELATED APPLICATIONS This application is a continuation-in-part of application Ser. No. 08/258,152 filed Jun. 10, 1994, now U.S. Pat. No. 5,686,279, which is a continuation-in-part of application Ser. No. 08/076,299, filed Jun. 11, 1993, now U.S. Pat. No. 5,834,256, the disclosures of both application are incorporated by reference in their entirety herein.

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L4: Entry 4 of 26 File: USPT Apr 18, 2000

DOCUMENT-IDENTIFIER: US 6051427 A
TITLE: Method for production of high titer virus and high efficiency retroviral mediated transduction of mammalian cells

DEPR:
In order to improve the poor retroviral gene transfer into hematopoietic stem cells by supernatant infection, recreation of the cell-cell contacts was attempted and resulted in higher efficiency of gene transfer (Morre et al., Blood 79:1393 (1992)). However, cocultivation of bone marrow cells on stroma is neither acceptable by the FDA nor is it economically feasible. Therefore, attempts at recreation of the cell cell contacts have been undertaken. The interaction of fibronectin on stromal cells and VLA-4 on hematopoietic stem cells (Williams et al., supra) has been previously demonstrated. By isolating the CS-1 domain of fibronectin responsible for this interaction and coating plates with this protein molecule, Moritz et al. demonstrated that retroviral gene transfer by supernatant infection can be significantly enhanced (J. Clin. Invest., 93:1451-1457 (1994)). This approach necessitates the isolation of significant quantities of proteolytic fragments from natural material. Furthermore, many molecules participate in the cell cell interactions of stroma and stem cells (Liesveld et al. Blood 81:112-121 (1993)).

DEPR:
Table 15 above also demonstrates that the use of fibronectin plates, in combination with the viruses of the instant invention, results in a higher efficiency of transduction of stem cells then that previously reported for other retroviral systems (Moritz et al. supra).

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L4: Entry 9 of 26 File: USPT Jun 9, 1998

US-PAT-NO: 5762926
DOCUMENT-IDENTIFIER: US 5762926 A
TITLE: Method of grafting genetically modified cells to treat defects, disease or damage of the central nervous system
DATE-ISSUED: June 9, 1998

US-CL-CURRENT: 424/93.21; 435/320.1, 435/375, 435/69.1, 514/44

APPL-NO: 8/ 464397
DATE FILED: June 5, 1995

PARENT-CASE:
CROSS-REFERENCE TO RELATED APPLICATIONS This application is a divisional application of U.S. Ser. No. 08/209,609, filed Mar. 10, 1994, which is a file wrapper continuation of U.S. Ser. No. 07/792,894, filed Nov. 15, 1991, now abandoned, which is continuation-in-part of U.S. Ser. No. 07/285,196 filed Dec. 15, 1988, now U.S. Pat. No. 5,082,670, the entire disclosure of which is expressly incorporated by reference herein.

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L4: Entry 10 of 26 File: USPT Nov 11, 1997

US-PAT-NO: 5686278
DOCUMENT-IDENTIFIER: US 5686278 A

TITLE: Methods for enhanced retrovirus-mediated gene transfer

DATE-ISSUED: November 11, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Williams; David A.	Indianapolis	IN	N/A	N/A
Patel; Vikram P.	Olney	MD	N/A	N/A

US-CL-CURRENT: 435/456; 435/372

CLAIMS:

What is claimed is:
1. A method for increasing the frequency of transduction of hematopoietic cells by a replication-defective recombinant retrovirus vector, comprising infecting hematopoietic cells with a replication-defective recombinant retrovirus vector in the presence of substantially pure fibronectin, substantially pure fibronectin fragments, or a mixture thereof, so as to increase the frequency of transduction of the hematopoietic cells by the retrovirus vector.
2. The method of claim 1 wherein the hematopoietic cells have a protein deficiency or abnormality and the recombinant retrovirus vector includes an exogenous gene encoding the protein.
3. The method of claim 1 wherein the cells are infected with the retrovirus vector in the presence of a fibronectin fragment containing the alternatively spliced CS-1 cell adhesion domain.
4. The method of claim 1 wherein the hematopoietic cells are a human hematopoietic cellular population including human stem cells.
5. The method of claim 2 wherein the exogenous gene is a gene encoding adenosine deaminase.
6. The method of claim 5 wherein the exogenous gene is a gene encoding human adenosine deaminase.
7. The method of claim 4 wherein the hematopoietic cells are adherent-negative, low density, mononuclear cells.
8. A method for producing transduced hematopoietic cells, comprising:
infecting hematopoietic cells in culture with a replication-defective recombinant retrovirus in the presence of immobilized fibronectin, immobilized fibronectin fragments, or an immobilized mixture thereof, to produce transduced hematopoietic cells.
9. The method of claim 8 which includes harvesting the transduced hematopoietic cells.
10. The method of claim 8 wherein the hematopoietic cells have a protein deficiency or abnormality and the recombinant retrovirus vector includes an exogenous gene encoding the protein.
11. The method of claim 8 wherein the hematopoietic cells have an enzyme deficiency or abnormality and the exogenous gene is a gene encoding the enzyme.
12. The method of claim 11 wherein the hematopoietic cells are human hematopoietic cells having an enzyme deficiency or abnormality and the exogenous gene is a human gene encoding the enzyme.
13. The method of claim 11 wherein the hematopoietic cells have an adenosine deaminase deficiency and the exogenous gene encodes adenosine deaminase.
14. The method of claim 12 wherein the human hematopoietic cells have an adenosine

deaminase deficiency and the exogenous gene encodes adenosine deaminase.
15. The method of claim 12 wherein the cells are infected with the retrovirus in the presence of an immobilized fibronectin fragment containing the alternatively spliced CS-1 cell adhesion domain.
16. The method of claim 15 wherein the hematopoietic cells are a human hematopoietic cellular population including human stem cells.
17. The method of claim 16 wherein the hematopoietic cells are adherent-negative, low density, mononuclear cells.
18. A method for improving retroviral-mediated gene transfer in hematopoietic cells, comprising conducting the retroviral-mediated gene transfer in the presence of immobilized fibronectin, immobilized fibronectin fragments or an immobilized mixture thereof.
19. The method of claim 18 wherein the hematopoietic cells are a mammalian hematopoietic cellular population including mammalian stem cells.
20. A composition comprising:
a viable hematopoietic cellular population transduced by retroviral-mediated gene transfer; and
immobilized fibronectin, immobilized fibronectin fragments, or an immobilized mixture thereof, in the presence of which said population has been transduced by the retroviral-mediated gene transfer;
said composition being free from virus-producing cells.
21. The composition claim 20 wherein the cellular population is a human hematopoietic cellular population including human stem cells.
22. The composition of claim 20 wherein the hematopoietic cellular population is comprised of adherent-negative, low-density mononuclear cells.

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L4: Entry 14 of 26 File: EPAB Nov 11, 1997

PUB-NO: US005686278A
DOCUMENT-IDENTIFIER: US 5686278 A
TITLE: Methods for enhanced retrovirus-mediated gene transfer

PUBN-DATE: November 11, 1997

INVENTOR-INFORMATION:

NAME	COUNTRY
WILLIAMS, DAVID A	US
PATEL, VIKRAM P	US

INT-CL (IPC): C12N 15/09; C12N 5/10
EUR-CL (EPC): A01K067/027; A61K047/48, A61K048/00 , C07K014/78 , C12N005/10 , C12N009/78 , C12N015/86

ABSTRACT:

A method to increase the efficiency of transduction of hematopoietic cells by retroviruses includes infecting the cells in the presence of fibronectin or fibronectin fragments. The fibronectin and fibronectin fragments significantly enhance retroviral-mediated gene transfer into the hematopoietic cells, particularly including committed progenitors and primitive hematopoietic stem cells. The invention also provides improved methods for somatic gene therapy capitalizing on the enhanced gene transfer, and hematopoietic cellular populations.

L4: Entry 25 of 26 File: DWPI Aug 9, 1990

DERWENT-ACC-NO: 1990-260942
DERWENT-WEEK: 199034

TITLE: Recombinant, homogeneous cellular fibronectin variants - prepd. by transfected cells contg. retroviral vector carrying specific DNA, useful in wound healing, etc.

INVENTOR: GUAN, J L; HYNES, R O

PRIORITY-DATA: 1989US-0305849 (February 2, 1989)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
WO 9008833 A	August 9, 1990	N/A	000	N/A

INT-CL (IPC): C07K 13/00; C12N 15/12; C12P 21/02

ABSTRACTED-PUB-NO: WO 9008833A
BASIC-ABSTRACT:

Prodn. of biologically active, homogeneous, recombinant cellular fibronectin (cFN) homodimer comprises introducing into a host cell a recombinant vector including full length cDNA for mammalian cFN, then culturing the resulting cells.

Also new are (1) recombinant cFN homodimer, which may lack the EIIIA or IIIB region; (2) recombinant retrovirus contg. the specified full-length cDNA and (3) recombinant cFN (homodimer or heterodimer) without the 25C-terminal amino acids of region V.

Specifically, the cells are transfected with recombinant retrovirus contg. the specified cDNA, so that the cells integrate this cDNA into their genome.

USE/ADVANTAGE - The recombinant cFN is useful in the same way as natural fibronectin, e.g. in tissue repair (esp. wound healing, where it stimulates cell migration, adhesion, etc.), nerve regeneration, control of haemostasis and thrombosis, etc. Unlike plasma fibronectin (which is an impure mixt. of variants), the new recombinant prods. can be prepd. as single pure variants.

In an example, pLJ-FN was introduced into the packaging cell line, psi 2, then the cells subjected to glycerol shock for transient expression of recombinant virus. The culture medium was recovered and used to infect 3T3 cells in presence of polybrene. After several days, the cells were grown on a medium contg. 0.5 mg/ml G418 and some of the survivors cloned by limiting dilution.

ABSTRACTED-PUB-NO: WO 9008833A
EQUIVALENT-ABSTRACTS:

CHOSEN-DRAWING: Dwg.0/9

L7: Entry 1 of 20 File: USPT Oct 31, 2000

DOCUMENT-IDENTIFIER: US 6140111 A
TITLE: Retroviral gene therapy vectors and therapeutic methods based thereon

DEPR:
Several different MFG-based vectors encoding the same gene product, human adenosine deaminase (huADA) and the same vector backbone, yet differing specifically in transcriptional control sequences were constructed and evaluated for their capacity to efficiently transduce murine hematopoietic stem cells. Transduced stem cells were subsequently used in bone marrow transplantation experiments, and the long term vector-mediated expression of huada by various hematopoietic cells following transplantation.

DEPR:
To investigate human adenosine deaminase (huADA) expression in cells derived from transduced hematopoietic stem cells in vivo, mice were transplanted with 2.5.times.10.sup.5 to 4.5.times.10.sup.6 BM cells that had been co-cultured with recombinant virus producing cells as described in Section 11.1.2., supra. Fifteen to eighteen mice were transplanted per construct. A first step in assessing vector mediated gene expression involved the analysis of huADA enzyme activity in the peripheral blood cells (PBC) of reconstituted animals 5-7 months after transplantation using the assay described in Section 11.1.3., supra (FIG. 12). In this assay, human ADA activity can be readily separated from the murine ADA activity and the relative levels of the two activities can be estimated by densitometry measurements of the intensity of labeled in situ reaction products. This assay generates signals proportional to the amount of enzyme activity.

DEPC:
11. EXAMPLE: IN VIVO EXPRESSION OF HUMAN ADENOSINE DEAMINASE BY HEMATOPOIETIC STEM CELLS TRANSDUCED WITH SEVERAL RECOMBINANT MFG-ADA RETROVIRAL VECTORS

ORPL:
Einerland, M.P.W. et al. "Factors Affecting the Transduction of Pluripotent Hematopoietic Stem Cells: Long-term Expression of a Human Adenosine Deaminase Gene in Mice". Blood 81: 254-263 (1993).

ORPL:
Lim, Bing et al. "Long-term expression of human adenosine deaminase in mice transplanted with retrovirus-infected hematopoietic stem cells". Proceedings of the National Academy of Sciences, USA 86: 8892-8896 (1989).

ORPL:
Wilson, James M. et al. "Expression of human adenosine deaminase in mice reconstituted with retrovirus-transduced hematopoietic stem cells". Proceedings of the National Academy of Sciences USA 87: 439-443 (1990).

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L7: Entry 15 of 20 File: USPT Sep 23, 1997

US-PAT-NO: 5670351
DOCUMENT-IDENTIFIER: US 5670351 A
TITLE: Methods and compositions for the ex vivo replication of human hematopoietic stem cells
DATE-ISSUED: September 23, 1997

US-CL-CURRENT: 435/440; 435/347, 435/366, 435/370, 435/372, 435/456

APPL-NO: 8/ 366493
DATE FILED: December 30, 1994

PARENT-CASE:
This is a Continuation of application Ser. No. 07/740,590 filed on Aug. 5, 1991, now U.S. Pat. No. 5,399,493, which was a continuation in part of application Ser. No. 07/628,343, filed on Dec. 17, 1990, now abandoned, which was a continuation-in-part of application Ser. No. 07/366,639, filed on Jun. 15, 1989, now abandoned, which was filed as International Application No. PCT/US90/03438, on Jun. 14/1990, and is a CIP of Ser. No. 07/737,024 filed Jul. 29, 1991, now abandoned.

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L7: Entry 19 of 20 File: USPT Apr 11, 1995

US-PAT-NO: 5405772
DOCUMENT-IDENTIFIER: US 5405772 A

TITLE: Medium for long-term proliferation and development of cells

DATE-ISSUED: April 11, 1995

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ponting; Ian L. O.	Woodland Hills	CA	N/A	N/A

US-CL-CURRENT: 435/378; 435/373, 435/395, 435/405, 435/406

CLAIMS:

What is claimed as new and desired to be protected by Letters Patent of the United States is:

1. A medium for the long-term proliferation and development of cells, which comprises the following ingredients in the indicated amounts: (a) a standard culture medium 0.8-1.09 x, (b) serum albumin 3-50 mg/ml, (c) transferrin 25-1000 ug/ml, (d) lipids and fatty acids 5-100 ug/ml, (e) cholesterol 3-30 ug/ml, (f) reducing agent 30-300 uM, (g) pyruvate 30-500 ug/ml, (h) nucleosides 5-30 ug/ml, (i) at least one growth factor selected from the group consisting of: (1) epidermal growth factor 5-200 ng/ml (2) fibroblast growth factor 0.5-40 ng/ml (3) platelet-derived growth factor 2-200 ng/ml; and (4) insulin 2-100 ug/ml. (j) at least one extracellular matrix material selected from the group consisting of: (1) collagen IV 2-100 ug/cm.sup.2 ; and (2) fibronectin 0.5-100 ug/cm.sup.2 ; wherein said medium for the long-term proliferation and development of cells is serum-free or serum-depleted and is capable of culturing cells comprising adipocytes, macrophages, endothelial cells, fibroblasts, and hematopoictic progenitor cells.

2. The medium according to claim 1, further comprising a glucocorticoid.

3. The medium according to claim 1, wherein said glucocorticoid is hydrocortisone.

4. The medium according to claim 1, further comprising stromal cells.

5. The medium according to claim 1, further comprising an inhibitor of CSF-1 activity.

6. The medium according to claim 1, wherein said cells to be cultured are incapable of producing CSF-1.

7. The medium according to claim 6, wherein said cells to be cultured are obtained from a B6C3Fe-a/a-op/op mouse strain.

8. The medium according to claim 1, wherein said standard culture medium is Iscove's Modified Dulbecco's Medium.

9. The medium according to claim 1, wherein said serum albumin, transferrin and growth factors are each of human, mouse or bovine origin.

10. The medium according to claim 1, wherein said nucleosides are one or more selected from the group consisting of adenosine, guanosine, cytidine, uridine, 2'-deoxyadenosine, 2'-deoxyguanosine, 2'-deoxycytidine and thymidine.

11. The medium according to claim 1, wherein all of said extracellular matrix materials are included.

12. The medium according to claim 1, wherein said cells are hematopoietic or lymphopoietic.

lymphopoietic.
13. The medium according to claim 1, wherein said cells are from mammalian organs or tissues.
14. The medium according to claim 1, wherein said cells are primary cells or cell lines.
15. A method of long-term culture of cells which comprises culturing the cells for 8 to 20 weeks in the medium according to claim 1.
16. A method of short-term culture of cells which comprises culturing the cells for 2 to 7 weeks in the medium according to claim 1.